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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/258,947	03/01/99	MILLER J	011.00117

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EXAMINER	
CLEMENS,K	
ART UNIT	**PAPER NUMBER**
1644	12

DATE MAILED: 11/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/258,947	Applicant(s) MILLER ET AL.	
	Examiner Karen Clemens	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2000* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1-6,8 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☒ The proposed drawing correction filed on *01 March 1999* is: a)☒ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3/8/00* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. The Examiner of your application in the Patent and Trademark Office has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Karen Clemens in Art Unit 1644, Technology Center 1600 ((703) 308-8365).

2. This application is a continuation-in-part of application Serial No. 08/556,597, now U.S. Patent 5,877,155, which is a continuation-in-part of application Serial No.08/406,330, now U.S. Patent 5,817,748.

3. Claims 1-10 are currently pending.

4. Applicant's election of Group III, Claims 7 and 9, and species election of SEQ ID NO:174 wherein amino acid 3 is tyrosine and amino acid 4 is arginine, in Paper No. 11, filed 10/10/00 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-6, 8 and 10 and the nonelected species of Group III (SEQ ID NO:174 wherein amino acid 3 is alanine, asparagine, or glutamine or amino acid 4 is phenylalanine, serine or tryptophan) are withdrawn from further consideration by the Examiner as being drawn to nonelected inventions (see 37 C.F.R. §1.142(b)).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. §1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. §1.48(b) and by the fee required under 37 C.F.R. §1.17(h).

5. Claims 7 and 9 as they read on the elected species are currently under examination.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 7 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a molecule that inhibits ristocetin induced aggregation of platelets, identified by determining whether the molecule binds to an isolated peptide of SEQ ID NO:174, and which may have a three-dimensional structure complementary to the three dimensional structure of the said isolated peptide. The molecule or "anti-mimotope" is disclosed to be any suitable molecule such as an antibody, a second peptide, a carbohydrate, a DNA or an RNA molecule (see specification page 17 in particular).

However, Applicant's disclosure is limited to a set of peptides that were developed using the "mimotope decapeptide" (assumed to be SEQ ID NO:1) and includes peptides of SEQ ID NOs: 94-99 and 157-172 of which SEQ ID NO:94 has been found to inhibit ristocetin induced aggregation of platelets *in vitro*.

The specification fails to describe the requisite structural features of the other molecules such as the other peptides, antibodies, carbohydrates, DNA or RNA molecules that would render the claimed molecules able to inhibit ristocetin induced aggregation of platelets considered the essential feature of the instant invention. Therefore, applicant has not disclosed sufficient species such that one skilled in the art would conclude that applicant was in possession of the claimed genus of molecules that bind to SEQ ID NO:174, inhibit ristocetin induced aggregation of platelets and /or have the three dimensional structure complementary to the three dimensional structure of the peptide of SEQ ID NO:174.

Consequently, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See *Regents of the University of California v. Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)*. Also see the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1st "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 7 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for SEQ ID NOs:94, 104 and 105, which inhibits ristocetin induced aggregation of platelets *in vitro* and binds to a mimotope decapeptide (assumed to be SEQ ID NO:1), and for the peptide of SEQ ID NO:107 which represents the PT-vWD variant of GPIb (amino acids 228-237), which also inhibits ristocetin induced aggregation of platelets, does not reasonably provide enablement for all suitable molecules such as an antibody, other peptides, a carbohydrate, a DNA or an RNA molecule which bind to SEQ ID NO:174, inhibit ristocetin induced aggregation of platelets and/or have the three dimensional structure complementary to the three dimensional structure of the peptide of SEQ ID NO:174 (see specification page 17 in particular) . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. The specification discloses that SEQ ID NO:94, identified by binding to a mimotope decapeptide (assumed to be SEQ ID NO:1) which resembles the mAb C-34 binding site on GPIb, was found from a series of 46 similarly isolated clones to inhibit the ristocetin-induced aggregation of platelets *in vitro* (see specification, Figure 8 in particular) suggesting that the ability to bind to the mimotope decapeptide alone is insufficient to predict which peptides, or other suitable molecules such as antibodies, carbohydrates, DNA or RNA, are also able to inhibit the ristocetin-induced aggregation of platelets *in vitro.* Further, when SEQ ID NO:94 (RHVAWWRQGV) was modified by one amino acid (SEQ ID NO:104 - RHVAWWRQVV) the inhibition of ristocetin-induced aggregation of platelets was slightly reduced, when modified at a second amino acid the inhibition was significantly reduced (SEQ ID NO:106 RHVAWWKQGV), however, when modified at both sites (SEQ ID NO:105 RHVAWWKQVV) the peptide retained potent inhibitory activity (see page 17 and figures 9-11 in particular), suggesting that one skilled in the art would be unlikely to predict which molecules as broadly claimed would

bind to SEQ ID NO:174 (WRXXEY), inhibit ristocetin-induced aggregation of platelets and/or have the three dimensional structure complementary to the three dimensional structure of the peptide of SEQ ID NO:174.

The specification fails to provide sufficient guidance or working examples such that one skilled in the art could make and use all molecules as broadly claimed. The specification is silent with respect to specifically which structural elements are critical to the claimed functions and the methods necessary to predict which peptide, carbohydrate, antibody, DNA or RNA species would fall within the scope of the claims.

The current state of the art for the prediction of peptide function based on primary structure alone is inadequate (see Mayo). Analysis of the peptide structure alone may help to understand which specific amino acid residues promote a particular function but this is usually not the case (see Mayo, page 214, right column). Furthermore, It is not routine in the art to screen large numbers of peptides to determine which would possess the structural and functional criteria of the claimed molecules based on the instant disclosure. A skilled artisan would require guidance, such as information regarding the amino acid sequences required to preserve the biological, structural or functional features of the peptide in order to use the molecules in a manner reasonably commensurate with the scope of the claims. Therefore, it would take an undue amount of experimentation for one skilled in the art to make and use the molecules in a manner reasonably commensurate in scope with the claimed invention.

In view of the lack of sufficient guidance and limited working examples, the broad scope of the claim and the unpredictability of the art it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

8. The following is a quotation of the appropriate paragraphs of *35 U.S.C. § 102* that form the basis for the rejections under this section made in this Office action:

> "A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

Claims 7 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Miller et al. (*British J. Haematology* 74:313-319, 1990, see IDS, form 1449).

Miller et al. teach the monoclonal antibody C-34, which binds the GPIb/IX complex, and inhibits ristocetin induced aggregation of platelets. Monoclonal Ab C-34 would be expected to bind to SEQ ID NO:174, which was designed to mimic the eptiope to which the C-34 mAb binds. Therefore, the reference teachings thus anticipate the claimed invention.

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Clemens whose telephone number is (703) 308-8365. The examiner can normally be reached Monday through Friday from 8:00 am to 5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Karen Clemens, Ph.D.
Patent Examiner
Technology Center 1600
November 17, 2000

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